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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
10/032,728	12/28/2001	Albert H. Olivencia-Yurvati	073314.0102	6388

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EXAMINER
AFREMOVA, VERA

ART UNIT	PAPER NUMBER
1651	16

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/032,728	Applicant(s) Olivencia-Yurvati et al.
	Examiner Vera Afremova	Art Unit 1651

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Mar 2, 2003*.

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-18* is/are pending in the application.

4a) Of the above, claim(s) *1-6 and 18* is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *7-17* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

[illegible]

Attachment(s)

1)	Notice of References Cited (PTO-892)	4)	Interview Summary (PTO-413) Paper No(s).
2)	Notice of Draftsperson's Patent Drawing Review (PTO-948)	5)	Notice of Informal Patent Application (PTO-152)
3) [X]	Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4 and 6*	6)	Other

DETAILED ACTION

Applicants' election without traverse of the Group II invention (claims 7-17) in Paper No. 9 filed 3/03/2003 is acknowledged.

Claims 1-6 and 18 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 9 filed 3/03/2003.

Claims 7-17 are under examination in the instant office action.

Claim Objections

Claims 7-17 are objected to because of the following informalities:

Claim 7 contains some typing error, for example: after the phrase "cardioplegia" on line 4 phrase "solution" or "composition" appears to be missing. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 7-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the limitation "the cardioplegia solution" in step iv) in a process for performing cardiopulmonary bypass surgery. There is insufficient antecedent basis for this limitation in the claim. It is uncertain whether both steps ii) and iv) refer to the same

solution in step ii). Further, claims 8-12 and 14-16 are indefinite with regard to the limitation

"the cardioplegia solution" because it is uncertain as presently claimed whether these claims refer to the composition of step ii) in claim 7 or else.

In the instant office action the claimed process is interpreted as drawn to the use of "cardioplegia solution" comprising chemicals as in step ii).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hermann et al. [IDS-4 ref. QQ].

Claims are directed to a process for performing cardiopulmonary bypass surgery by administering a cardioplegia solution comprising pyruvate to the heart of a human patient in order to arrest the heart during the surgery. The claimed cardioplegia solution does not comprise NaCl, KCl, glucose, insulin, CaCl2 and lidocaine. Some claims are further drawn to diluting the cardioplegia solution with whole blood. Some claims are further drawn to the effects of administration of the pyruvate containing solution including effects such as protection of the heart from injury resulting from ischemia, rapid recovery of mechanical function, improved heart energy reserves, antioxidant action and inotropic support.

Hermann et al. discloses a process for performing cardiopulmonary bypass surgery by administering directly to the heart of a human patient a composition or a cardioplegia solution comprising pyruvate (see page 1321, col. 2, last paragraph) in order to arrest the heart during the surgery or in order to reduce the heart rate (page 1322, col. 2, lines 1-2). The reference discloses that the haemodymanic action of pyruvate composition has been reversed by providing a chemical stimulus with saline (page 1322, col. 2, par. 2) in order to resume heart rate or beating as encompassed by the claimed process. The reference teaches the same beneficial effects of administration of the pyruvate containing composition as encompassed by the presently claimed process (claims 12-14 and 17) including protection of the heart from injury resulting from ischemia, rapid recovery of mechanical function, optimization of energy production and inotropic support (page 1321, col. 2, par. 2). The cited reference teaches that administration of the pyruvate containing composition results in optimization or in stabilization of heart energy reserves (summary or page 1321, col. 2, par. 2) and, thus, it teaches or suggests neutralization of prooxidant compounds and maintenance of antioxidant components as encompassed by the presently claimed process (claims 15 and 16).

The cited reference by Hermann et al. teaches the use of pyruvate concentration in the starting cardioplegia solution such as 150 mM which is higher than the presently claimed concentration 0.2-50 mM in the process of administering the cardioplegia solution. However, the method of the cited reference encompasses [illegible] pyruvate containing composition as encompassed by the presently claimed process (claims 8-11) wherein

the final pyruvate concentration in the coronary arterial blood during cardiopulmonary bypass surgery in human patient in the method of the cited reference is about 3-6 mM (page 1322, col. 1, par. 1) which is within the claimed pyruvate concentration range (claim 7). Thus, although the particular sequences of steps as presently claimed and as disclosed in the cited reference are not identical, the therapeutically effective pyruvate amounts, which produce the same effects, are the same in the claimed method and in the cited method for performing cardiopulmonary bypass surgery in human patients.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to administer a pyruvate containing cardioplegia composition/solution during cardiopulmonary bypass surgery in human patients with a reasonable expectation of success in protecting the heart from injury resulting from ischemia, rapid recovery of mechanical function, stabilization of heart energy reserves, antioxidant action and inotropic support as taught and suggested by the prior art. It is considered to be within the purview of one having ordinary skill in the art to adjust the final concentration of therapeutically effective amounts of pyruvate as taught for the method for performing cardiopulmonary bypass surgery in human patients for the expected benefits of the pyruvate containing cardioplegia composition. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

[illegible] be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Claims 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/02653 [IDS-6 ref. H] taken with Rao et al. [IDS-6 ref. M], US 4,988,515 [IDS-4 ref. B], Hermann et al. [IDS-4 ref. QQ] and Tajero-Taldo et al. [IDS-4 ref. RR].

Claims are directed to a process for performing cardiopulmonary bypass surgery by administering a composition or a cardioplegia solution comprising 0.2-50 mM pyruvate, 0-250 mM NaCl, 0-250 mM KCl, 0-200 mM glucose, 0-200 U/L insulin, 0-20 CaCl2 mM and 0-2 g/L lidocaine to the heart of a human patient in order to arrest the heart during the surgery. Some claims are further drawn to dilution of cardioplegia composition with whole blood prior administration at ratio blood to solution such as 0.1-20 to 1. Some claims are further drawn to the effects of administration of the pyruvate containing composition including protection of the heart from injury resulting from ischemia, rapid recovery of mechanical function, stabilization of heart energy reserves, antioxidant action and inotropic support.

WO 93/02653 teaches a process for performing cardiopulmonary bypass surgery (example C, pages 19-20) by administering directly to the heart of human patient a composition or a cardioplegia solution which comprising 100-150 mM NaCl, 5-20 mM KCl, 0.5-30 mM CaCl2, 5-300 mM glucose, pyruvate 5-100 mM and 0.1-0.5 mM lidocaine (table 1, page 11) wherein concentrations of components are within the ranges as required by the presently claimed method. The particular example of clinical open-heart surgery as disclosed by the cited WO

[illegible]

1).

The cited WO 93/02653 is lacking disclosure related to incorporation of insulin in the cardioplegia solution during cardiopulmonary bypass surgery. However, the reference by Rao et al teaches a process for performing cardiopulmonary bypass surgery wherein the cardioplegia solution comprises 10 IU/L insulin (abstract) as a beneficial component which provides for myocardial metabolic and functional recovery (abstract) of patients in need of cardiopulmonary bypass surgery.

The cited references WO 93/02653 and Rao et al are silent with regard to dilution of the cardioplegia solution with blood before administration of the cardioplegia solution.

However, US 4,988,515 teaches a process for performing cardiopulmonary bypass surgery wherein the cardioplegia solution is mixed with blood in the ratio blood to concentrated solution 4:1 (col. 4, lines 15-20). The cited patent also suggests to use the pyruvate containing cardioplegia solution (col. 4, line 5) for performing cardiopulmonary bypass surgery.

In addition, the cited references Hermann et al. [IDS-4 ref. QQ] and Tajero-Taldo et al. [IDS-4 ref. RR] are relied upon to demonstrate the beneficial effects of the pyruvate containing composition or cardioplegia solutions in the method for performing cardiopulmonary bypass surgery and perfusion of isolated hearts. For example: the reference by Hermann et al teaches beneficial effects of administration of the pyruvate containing composition including protection of the heart from injury resulting from ischemia, rapid recovery of mechanical function, stabilization of heart energy reserve and inotropic support in the method of performing cardiopulmonary bypass surgery as explained above. The reference by Tajero-Taldo et al is relied

upon for the disclosure of antioxidant action of the pyruvate containing composition or cardioplegia solutions in the method comprising heart perfusion with cardioplegia solution (abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to combine chemical components of cardioplegia solution including pyruvate, NaCl, KCl, glucose, insulin, CaCl2 and lidocaine at concentration as taught and/or suggested by the cited references WO 93/02653 [IDS-6 ref. H] and Rao et al. [IDS-6 ref. M] in the method for performing cardiopulmonary bypass surgery in human patients with a reasonable expectation of success because it is well known that it is prima facie obvious to combine ingredients which are taught by the prior art to be useful for the same purpose of performing cardiopulmonary bypass surgery in human patients in order to form a composition which is useful for the same purpose. The idea for combining the known components flows logically from their having been used separately in the prior art. In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). One of skill in the art would have been motivated to incorporate pyruvate in the cardioplegia solution in the method for performing cardiopulmonary bypass surgery in human patients for the expected benefits in protecting the heart from injury resulting from ischemia, and recovery of mechanical function, stabilization of heart energy reserve, antioxidant action, and inotropic support as taught and suggested by the prior art [Hermann et al. [IDS-4 ref. QQ]

and Tajero-Taldo et al. [IDS-4 ref. RR]}. It is considered to be within the purview of one having ordinary skill in the art to adjust the final concentration of therapeutically effective amounts of cardioplegia solution by mixing blood with a concentrated cardioplegia solution in the method for performing cardiopulmonary bypass surgery in human patients as taught by US 4,988,515 [IDS-4 ref. B]. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

SANDRA E. SAUCIER
PRIMARY EXAMINER

April 30, 2003.

VA

Information Disclosure Statement

The information disclosure statement filed 4/03/2002 has been considered. However the reference UU is not a prior art reference suitable for PTO Form 1449 and for printing on the face of the issued patent. For this reason the citation has been crossed out.

Drawings

Formal drawings filed 12/17/202 have been approved by examiner and draftsmen.

VH